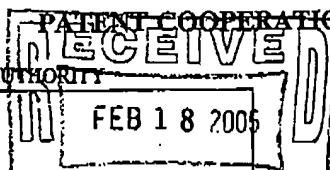


From the
INTERNATIONAL SEARCHING AUTHORITY

PATENT COOPERATION TREATY



PCT

To:
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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

15 FEB 2005

Applicant's or agent's file reference

PR60317WO

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/19692

International filing date (day/month/year)

18 June 2004 (18.06.2004)

Priority date (day/month/year)

19 June 2003 (19.06.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C07D 403/12; A61K 31/416 and US Cl.: 544/316; 514/274

Applicant

SMYTHKLINE BEECHAM CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/19692

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/19692

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-72</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-72</u>	YES
	Claims <u>NONE</u>	NO
Industrial applicability (IA)	Claims <u>1-72</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-72 meet the criteria of novelty and inventive step set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instant compounds. EP 1223170 in the analogous art teaches a large genus of pyrimidine compounds that are useful as pharmaceutical agents, see formula (I) wherein R₁ or R₄ can be a heterocycle. The reference compounds further contain a -X-Y-R₂ group attached at the 4-position of the pyrimidine wherein X is an oxygen atom, a nitrogen atom or a sulfur atom. The instant claims are drawn to pyrimidine compounds wherein A is not a group which is analogous to the -X-Y-R₂ of the reference. The reference compounds does not specifically teach or fairly suggest pyrimidine compounds having the combination of substituents of the instant claims and therefore, one of ordinary skill in the art would not have been motivated to choose the instantly claimed pyrimidine compounds from the reference disclosed genus.

Claims 1-72 meet the criteria set out in PCT Article 33(4) because the compounds are disclosed to have pharmaceutical activity, and thus meet the requirement of industrial applicability because the subject matter claimed can be made or used in industry.